17 cases no candida or other fungal species was isolated, and amphotericin treatment was empirical. In 14 out of 21 courses an amphotericin dosage of 1 mg/kg/day had been achieved by the third day of treatment. Full dosage escalation was not possible in five courses because of pre-existing renal impairment, and two patients died within 72 hours of starting antifungal treatment.

Complete abolition of fever, defined as temperature equal to or less than 37°C for at least 10 days, was achieved within 48 hours of starting 13 of the 21 courses of amphotericin. Each seemed to be a genuine response to amphotericin in that no other explanation—for example, response to recent change of antibacterial regimen, addition of antiviral agent, or return of neutrophil counts towards normal values—was forthcoming Furthermore, the responders were more likely than non-responders to have other diagnostic features of systemic candidiasis: blood cultures positive for candida (four out of 13 compared with none out of eight); and cultures from other sites positive for candida (six out of nine compared with three out of eight). Mortality was lower among responders than non-responders: death within one month of starting amphotericin occurred in three out of 13 compared with three out of eight.

Odds introduced the concept of high and low stringency diagnosis of systemic candidiasis in a recent monograph.[2] How stringency may be diagnosed when a feverish, neutropenic patient with blood cultures or biopsy specimens yielding negative results and non-blood cultures that may or may not be positive for candida has failed to respond to adequate antibacterial treatment. Many patients treated with intravenous amphotericin in this context will fall into this category. The toxicity of amphotericin, particularly when used in combination with other nephrotoxic agents is considerable. The mortality from systemic candidiasis is high. Clearly in such uncertain circumstances any additional diagnostic clue—for example, complete abolition of fever within 48 hours of starting amphotericin—is beneficial.

Failure to reduce body temperature in 48 hours may be equally informative—it should prompt a continuation of the search for a bacterial or viral pathogen combined with further adjustments of the antimicrobial regimen. It can also be taken as a failed therapeutic trial of amphotericin, and consideration can be given to early discontinuation of antifungal treatment.

The rapid abolition of fever seen in some cases of undiagnosed fever on starting amphotericin treatment is an important diagnostic criterion for systemic candidiasis and should increase confidence in continuing amphotericin for a full course: in our practice 14 days at 1mg/kg/day.

S V DAVIES
J A MURRAY

Selly Oak Hospital,
Birmingham B29 6JD

1 Kinsey SE, Giles FJ, Holton J. Cusum plotting of temperature charts for assessing antimicrobial treatment in neutropenic patients. *Br Med J* 1989;**299**:775-6. (23 September.)
2 Odds FC. *Candida and candidosis*. 2nd ed. London: Baillière Tindall, 1988.

## Mumps viruses and mumps, measles, and rubella vaccine

SIR,—Correspondence has recently appeared in this journal[1-3] and others[4-7] concerning neurological reactions possibly associated with mumps following immunisation of children with measles, mumps, and rubella vaccine. We have developed a method for differentiating mumps virus strains that has been used to examine viruses isolated from people who have been vaccinated (technical details will be reported elsewhere). Briefly, a small region of the mumps viral genome is amplified in a polymerase chain reaction and the nucleotide composition determined by sequence analysis. Over a region of about 100 nucleotides we have found up to 5% differences occurring between virus strains. This has shown that the Jeryl Lynn and Urabe vaccine strains of mumps are different from each other and from wild type mumps viruses not associated with vaccination. Viruses isolated from patients with meningitis and parotitis in Britain[4-6] and Canada[8] that occurred after vaccination with the Urabe strain were identical to the Urabe strain over the region of the genome examined (table).

*Characterisation of mumps viruses isolated from patients with parotitis and meningitis after immunisation with Urabe mumps vaccine and from cases not associated with vaccine*

| Source | Clinical condition | Site of isolation | Type of virus |
|---|---|---|---|
| | | *Not associated with vaccine* | |
| Bristol | Parotitis | Throat | Wild-like |
| Edinburgh | Meningitis | Cerebrospinal fluid | Wild-like |
| Edinburgh | Sore throat | Nose and throat | Wild-like |
| London | Parotitis | Saliva | Wild-like |
| Canada | Parotitis | Throat | Wild-like |
| Canada | Parotitis | Throat | Wild-like |
| | | *Occurring after vaccination* | |
| Edinburgh | Meningitis | Cerebrospinal fluid | Urabe-like |
| Nottingham | Meningitis | Cerebrospinal fluid | Urabe-like |
| Canada | Parotitis | Throat | Urabe-like |
| Canada | Parotitis | Throat | Urabe-like |
| Canada | Parotitis | Throat | Urabe-like |
| Canada | Meningitis | Cerebrospinal fluid | Urabe-like |
| Canada | Meningitis | Cerebrospinal fluid | Urabe-like |
| Canada | Meningitis | Cerebrospinal fluid | Urabe-like |

We think that it is important that patients with mumps, especially those with neurological sequelae that are temporally associated with vaccination, be investigated fully. Virus should be isolated and characterised before a link with the vaccine is confirmed.

TIMOTHY FORSEY
PHILIP D MINOR

Division of Virology,
National Institute for Biological Standards and Control,
South Mimms,
Hertfordshire EN6 3QG

1 Crowley S, Al-Jawed ST, Kovar IZ. Mumps, measles, and rubella vaccination and encephalitis. *Br Med J* 1989;**299**:660. (9 September.)
2 Campbell AGM. Mumps, measles, and rubella vaccination and encephalitis. *Br Med J* 1989;**299**:916. (7 October.)
3 Begg NT, Noah ND. Mumps, measles, and rubella vaccination and encephalitis. *Br Med J* 1989;**299**:978. (14 October.)
4 Gray JA, Burns SM. Mumps meningitis following measles, mumps and rubella immunisation. *Lancet* 1989;ii:98.
5 von Muhlendahl KF. Mumps meningitis following measles mumps and rubella immunisation. *Lancet* 1989;ii:394.
6 Murray MW, Lewis MJ. Mumps meningitis after measles, mumps and rubella vaccination. *Lancet* 1989;ii:677.
7 Ehrengut W. Mumps vaccine and meningitis. *Lancet* 1989;ii:751.
8 Hockin JC, Furesz J. Mumps meningitis, possibly vaccine related—Ontario. Comment. *Canadian Diseases Weekly Report* 1988;**14**:210.

## Cervical intraepithelial neoplasia in general practice

SIR,—Like Dr D B Johnson and Mr C J Rowlands in Brecon[1] we have been conducting a systematic call and recall programme for cervical cytology since 1984. In a deprived inner city environment (Jarman score 20-50) our programme has been led by a health promotion nurse and assisted by computer.[2] We have 2531 women at risk (aged 20 to 64 with an intact uterus) in a total practice population of 9500. We have also achieved a smear rate of 78% in these women over the five years

*Results of smear tests in London and Brecon over five years*

| Age range | No with smear test | No (%) with cervical intraepithelial neoplasia: Grade I | Grade II | Grade III | Grade IV or above |
|---|---|---|---|---|---|
| 20-39 | 1318 | 17 (1·3) | 27 (2·0) | 35 (2·7) | 62 (4·7) |
| 40-64 | 668 | 8 (1·2) | 1 (0·1) | 16 (2·4) | 17 (2·5) |
| Total | 1986 | 25 (1·6) | 28 (1·4) | 51 (2·6) | 79 (4·0) |
| Brecon | 3012 | 47 (1·6) | 37 (1·2) | 52 (1·7) | 89 (3·0) |

1984-8. We have been more successful in younger women, having taken smears from 86% (1318/1528) of the 20-39 year olds but only 67% (668/1003) of the 40-64 year olds. Compare our rates of abnormal smear results with those in Brecon.

The incidence of cervical intraepithelial neoplasia grades I and II (mild and moderate dyskaryosis) is broadly the same as in Brecon, but our incidence of cervical intraepithelial neoplasia grade III (severe dyskaryosis and carcinoma in situ) is some 50% higher, which makes our incidence of cervical intrepithelial neoplasia grade II or worse some 33% higher.

We are concerned that both of our practices have failed despite much effort and high levels of practice organisation to meet the government's target of 80% uptake. If practices should decide that these levels are unachievable and abandon the exercise then government policy will be condemning large numbers of women to run the risk of having undiagnosed and hence untreated disease.

KAMBIZ BOOMLA
JOHN ROBSON
SHARON FITZPATRICK

Chrisp Street Health Centre,
London E14 6PG

1 Johnson DB, Rowlands CJ. Diagnosis and treatment of cervical intraepithelial neoplasia in general practice. *Br Med J* 1989;**299**:1083-6. (28 October.)
2 Robson J, Boomla K, Fitzpatrick S, *et al.* Using nurses for preventive activities with computer assisted follow up: a randomised controlled trial. *Br Med J* 1989;**298**:433-6.

## "Achieving a balance" and meeting the "safety net"

SIR,—The findings of the North West Thames regional paediatric advisory subcommittee[1] should come as no surprise. Many of us for many years have appreciated that a modern paediatric service cannot be delivered safely or efficiently from the large number of sites at present operating in many regions. Even if enough doctors and nurses were available and resources were ample many smaller hospitals would not provide the throughput to allow necessary modern skills to be either maintained or developed. This would neither be safe for patients nor provide adequate training for junior medical, paramedical, and nursing staff.

This is now accentuated by work on the safety net review. In North East Thames the review in paediatrics showed similar findings to those of Dr S A M Jones and her colleagues. Paediatric services are currently provided on 26 sites over 16 districts. Neonatal intensive care services at level 2 (sub-regional and above) are planned for seven sites. Our work on safe levels of staffing examined the feasibility not only of teams of three doctors at each level of cover, producing a one in three rota maintained by employing locum staff, but also of teams of four at each level, producing a one in four rota and enabling one in three to be achieved internally, which also goes some way to meeting the latest guidance on improving hours of work. The results suggested that if the region is to stay within current manpower constraints and to meet the level of staffing projected by the Joint Planning Advisory Committee there will be insufficient